REMARKS

Reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 1-12 are pending in the application.

Restriction Requirement

Claims 2-12, which were added by the Amendment and Reply filed August 22, 2005, have been withdrawn pursuant to a restriction requirement for allegedly being drawn to subject matter that is not related to the subject matter of claim 1. The restriction requirement is respectfully traversed.

Claim 1 recites an isolated nucleic acid sequence serving as a genetic regulatory element in a chimeric gene, wherein said DNA sequence is the intron of the 5' non-translated region of a plant H3.3 histone gene. Claim 12 recites a chimeric gene comprising a promoter, an intron derived from the 5' non-translated region of a plant H3.3 histone gene, and a coding sequence.

Whether denominated as an intron serving as a genetic regulatory element in a chimeric gene, or a chimeric gene comprising the intron, it is clear that claim 1 and claim 12 are directed to nucleic acid molecules comprising the intron of the 5' non-translated region of a plant H3.3 histone gene in the position of a regulatory element in a chimeric gene. Claim 11 is directed to the product of obtaining elements of a chimeric gene, including those listed in claim 12 and assembling those elements in sequence to form the claimed nucleic acid. It is impossible to conceive of a search strategy for these claims that would be mutually exclusive

or how there could possibly be a **serious** burden imposed upon the examiner in examining these claims together.

Claims 2-10 are directed to methods which can only result in the production of a nucleic acid in which the recited intron is serving as a genetic regulatory element in a chimeric gene as recited in claim 1or a chimeric gene within the scope of claim 12. Therefore, it is difficult to imagine a search strategy for these claims that would be mutually exclusive of the search of claims 1, 11, and 12 or how there could possibly be a serious burden imposed upon the examiner in examining this relatively limited number of claims together.

Applicants respectfully submit that this restriction requirement represents precisely the sort of hyper-technical, hair-splitting, restriction requirement that the policy set forth in Manual of Patent Examination Procedure § 803 was intended to avoid and indeed prohibits. "If the search and examination of all the claims in an application can be made without serious burden, the examiner **must** examine them on the merits, even though they include claims to independent or distinct inventions." Manual of Patent Examination Procedure § 803 (emphasis added).

The interests of the U.S. Patent and Trademark Office will not be served by forcing Office personnel to expend public resources to process multiple examinations of multiple applications containing these closely related claims, when there can be no serious burden in examining the limited number of claims now pending in the present application, particularly considering that the issues in the application are well developed. Furthermore, the interests of the public cannot be served by the Office issuing multiple patents directed to such closely related subject matter.

For at least the foregoing reasons, withdrawal of the restriction requirement and examination of claims 1-12 in the present application is appropriate and is requested.

In the present Office Action, two rejections of claim 1 under 35 U.S.C. § 112, first paragraph, have been maintained. These rejections are traversed in detail below. Reasons why these rejections cannot reasonably be applied to claims 2-12, which the Office has never addressed, were presented in Applicants' Amendment and Reply filed August 22, 2005. For Example, it is clear that the specification, when taken with what would have been known at the time the application was filed, describes and enables a person of ordinary skill in the art to carry out every step of the recited processes. It is furthermore well established that a product may be described by its manner of making, so that claim 11 is likewise described and enabled. Given these facts, Applicants respectfully submit that there can be no reason adduced that would explain why the specification that describes and enables claim 11, does not also describe and enable claims 12 and 1.

Turning now to the substance of the present Office Action, Applicants provide the following additional remarks.

Rejections under 35 U.S.C. § 112, first paragraph, written description

Claim 1 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to convey that the inventors had possession of the claimed invention at the time the application was filed. This rejection is respectfully traversed.

The only apparent basis that the Examiner has asserted for maintaining the rejection continues to be an allegation that Applicants have not defined the size or size range of the 5' region in which the expected 5' intron would occur. Applicants have pointed out that

Sinibaldi demonstrate that one of ordinary skill in the art knew how to recognize introns within genes. *See, e.g.*, Sinibaldi and Mettler, *Progress in Nucleic Acrid Research and Molecular Biology,* 42:229-57 (1992) (previously cited by the Office). Thus, the term "intron" would have inherently conveyed a description of a genetic element having certain structural features to a person of ordinary skill in the art at the time the application was filed and still does.

Applicants further pointed out that Chaubet et al., *J. Mol. Biol.* 225:559-74 (1992) (previously made of record), teaches that polypeptide sequences identical to those encoded by the two *Arabidopsis* genes from which the two introns of Example 2 of the Specification are derived has also been deduced from an alfalfa cDNA and a barley cDNA. Thus, one of ordinary skill in the art would have known of additional plant H3.3 genes in other species. *Id.* Both the Specification and the Chaubet et al. publication (which is referenced in the Examples of the Specification) teach that the first intron of a plant H3.3 gene can be found between the promoter sequence and the initiation codon of the gene. Thus, the teaching of the specification combined with what was known in the art combine to provide a description of representative species of the intron which serves as a genetic regulatory element of a chimeric gene in the claimed nucleic acid.

In response to Applicants' traversal, the Examiner has cited excerpts of Sinibaldi, taken out of the context of the paper as a whole, which are purported to teach that "there is variability among different introns, even within the same gene." However, the variability that Sinibaldi has remarked upon has not prevented the authors from identifying splice junctions, to align them, and to identify consensus sequences based upon those alignments (from 218 monocot introns and 505 dicot introns). This alignment could be performed by any computer-based alignment program and would have been readily available to permit a person

of ordinary skill in the art to recognize the introns recited in the claims. Furthermore, the reference sequences exemplified in the specification could be used as a guide to structures, since the variability of the first intron from the non-translated '5 region of plant H3.3 genes would be expected to be very much less variable than the full range of every intron from any gene that Sinibaldi is referring to.

Upon consideration of the specification in view of the state of the art as a whole, the Examiner's alleged basis for maintaining the rejection can not stand. The rejection has been traversed so that withdrawal of the rejection is appropriate and is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph, enablement

Claim 1 has been rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed.

Applicants have provided evidence that a person of ordinary skill in the art could identify and obtain a 5' intron of any plant H3.3 gene using routine methods demonstrated and taught by the specification and Chaubet et al., *supra*, in the exemplary sequence alignments that were provided as Attachment A of the Amendment and Reply filed November 2, 2004.

The Examiner complains that the sequence alignments that were provided as evidence are alignments of amino acid sequences. However, this objection provides no basis for rejecting Applicants' evidence and argument. The sequence alignments demonstrate the similarity between H3.3 genes, which would permit a person of ordinary skill in the art to recognize H3.3 genes. The intron of the 5'region of a plant H3.3 gene can be recognized by conserved consensus sequences as illustrated by Sinibaldi et al., *supra*. Furthermore, the fact that the alignments to rice and vine are to sequences dated 2003 and 2004 is immaterial to the

point that the alignments prove, namely that the sequences of histone H3.3 genes are conserved across species and therefore the two reference sequences that are exemplified in the specification provide sufficient information for a person of ordinary skill to recognize histone H3.3 genes. The specification was sufficient at the time that it was filed.

Example 2 of the specification teaches how to obtain the component material for the chimeric gene recited in claim 1. The DNA from which the exemplary introns were derived was obtained as described by Chaubet et al. The Chaubet et al. reference describes the identification of two histone H3.3-like genes using a labeled coding sequence of a histone gene from maize as a probe and also shows that genes encoding identical proteins appear in other plants and state as an example that the nucleic acid homology of the coding sequences compared to alfalfa is 80%.. Chaubet et al., *supra* at 570. The Chaubet et al. reference explains how the intron can be recognized by reference to conserved spice sites sequences. *Id.*

Given the teaching of Chaubet et al. and the Specification, a person of ordinary skill in the art could obtain any other plant histone H3.3 gene. The exhibits that Applicants previously provided have further demonstrated identical encoded sequences in vine and rice. Given this degree of homology and the nucleotide level homology taught by Chaubet et al., one would expect to be able to clone these and other corresponding H3.3-like genes using only routine methods and probes comprising these highly conserved sequences as taught by the Specification and the Chaubet et al. reference. Sequencing, cutting, linking and other manipulations could likewise be carried out using routine methods. It should be noted that under similar circumstances in *Capon*, *supra*, the Board of Patent Appeals and Interferences presumed and the Federal Circuit did not overturn this presumption. *Capon,* at 15.

In view of the highly conserved nature of plant histone H3.3 genes at both the amino acid and nucleic acid levels, the teachings of the specification and the art, and the level of ordinary skill in the art, a person of ordinary skill could have made and used the full scope of the claimed invention without undue experimentation. Accordingly it is appropriate to withdraw the enablement rejection of claim 1 under 35 U.S.C. § 112, first paragraph, and such action is respectfully requested.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY P.C.

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By: _____
Christopher L. North
Registration No. 50,433

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620